US007771736B2

(12) **United States Patent**
Abraham

(10) **Patent No.: US 7,771,736 B2**
(45) **Date of Patent: Aug. 10, 2010**

(54) **GLYPHOSATE FORMULATIONS AND THEIR USE FOR THE INHIBITION OF 5-ENOLPYRUVYLSHIKIMATE-3-PHOSPHATE SYNTHASE**

(75) Inventor: **William Abraham**, Wildwood, MO (US)

(73) Assignee: **Monsanto Technology LLC**, St. Louis, MO (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1466 days.

(21) Appl. No.: **10/652,684**

(22) Filed: **Aug. 29, 2003**

(65) **Prior Publication Data**

US 2004/0077608 A1 Apr. 22, 2004

Related U.S. Application Data

(60) Provisional application No. 60/407,032, filed on Aug. 30, 2002.

(51) **Int. Cl.**

A01N 57/02	(2006.01)
A01N 25/00	(2006.01)
A01N 57/18	(2006.01)
A01N 37/00	(2006.01)
A01N 37/12	(2006.01)
A01N 37/44	(2006.01)
A01N 35/08	(2006.01)

(52) **U.S. Cl.** **424/405**; 504/206; 514/563; 514/574

(58) **Field of Classification Search** ..... None
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,903,297	A		9/1975	Robert
3,977,860	A	*	8/1976	Franz 504/206
5,863,863	A	*	1/1999	Hasebe et al. 504/358
5,877,186	A		3/1999	Leef et al.

OTHER PUBLICATIONS

MedlinePlus: Medical Encyclopedia: AIDS Apr. 14, 2004.*

Roberts, et al. Evidence for the Shikimate pathway in apicomplexan parasites Nature 1998, 393, 801-805.*

Pudney "Antimalarial: From Quinine to Atovaquone" Fifty Years of Antimicrobial: Past Perspectives and Future Trends (Cambridge Society for General Microbiology, 53rd Symposium, 1995) pp. 229-247.

Ream et al. "EPSP Synthase: Binding Studies Using Isothermal Titration Microcalorimetry and Equilibrium Dialysis and Their Implications for Ligand Recognition and Kinetic Mechanism" Biochemistry, vol. 31, No. 24 (1992) pp. 5528-5534.

Stokkermans et al. "Inhibition of *Taxoplasma gondii* Replication by Dinitroaniline Herbicides" Experimental Parasitology, vol. 84 (1996) pp. 355-370.

Hackstein et al. "Parasitic Apicomplexans Harbor a Chlorophyll a-D1 Complex, the Potential Target for Therapeutic Triazines" Parasitology Research, vol. 81 (1995) pp. 207-216.

Schmidt et al. "*Phylum Apicomplexa*: Malaria and Piroplasms" Foundations of Parasitology. St. Louis, Times Mirror/Mosby (1985) pp. 149, 173-178.

Du et al. "Characterization of *Streptococcus pneumoniae* 5-enolpyruvylshikimate 3-phosphate synthase and its activation by univalent cations" Eur. J. Biochem., vol. 267 (2000) pp. 222-227.

Roberts et al. "Evidence for the shikimate pathway in apicomplexan parasites" Nature, vol. 393 (Jun. 25, 1998) pp. 801-805.

Leech et al. "Mutagenesis of Active Site Residues in Type I Dehydroquinase from *Escherichia coli*" J. of Biological Chem., vol. 270, No. 43 (Oct. 27, 1995) pp. 25827-25836.

Ridley "Planting new targets for antiparasitic drugs" Nature Medicine, vol. 4, No. 8 (Aug. 1998) pp. 894-895.

Gallay et al. "Progress in cloning, expression and purification of 5-enolpyruvylshikimate-3-phosphate synthase from patohgens causing meningitis" Biochemical Society Transactions, vol. 25, No. 4 (Nov. 1997) p. S632.

Coombs et al. "Recent advances in the search for new anti-coccidial drugs" International Journal for Parasitology, vol. 32, No. 5 (May 2002) pp. 497-508.

Du et al. "Synergistic Inhibitor Binding to *Streptococcus pneumoniae* 5-Enolpyruvylshikimate-3-phosphate Synthase with Both Monovalent Cations and Substrate" Biochemistry, vol. 39, No. 33 (2000) pp. 10140-10146.

McConkey "Targeting the Shikimate Pathway in the Malaria Parasite *Plasmodium falciparum*" Antimicrobial Agents and Chemotherapy, vol. 43, No. 1 (Jan. 1999) pp. 175-177.

* cited by examiner

Primary Examiner—Ernst V Arnold
(74) *Attorney, Agent, or Firm*—Senniger Powers LLP; James E. Davis

(57) **ABSTRACT**

Protozoan parasites of the phylum Apicomplexa include some of the most important causative agents of human and animal diseases, in particular, malaria. The discovery that an organelle found inside parasites of this phylum probably stems from a plastid of plant origin has stimulated research on the effect of chemical herbicidal agents on Apicomplexa. Importantly, the growth of these parasites can be inhibited by the herbicide glyphosate, suggesting that the shikimate pathway will make a good target for the development of new anti-parasite agents. The present invention discloses the use of the herbicidal agent glyphosate in combination with the polyvalent anion oxalic acid for the prevention and therapy of these pathogenic infections.

8 Claims, 2 Drawing Sheets